DNM2 gene

dynamin 2

Normal Function

The *DNM2* gene provides instructions for making a protein called dynamin 2. Dynamin 2 is present in cells throughout the body. It is involved in endocytosis, which is a process that brings substances into the cell. During endocytosis, the cell membrane folds around a substance (such as a protein) outside the cell to form a sac-like structure called a vesicle. The vesicle is drawn into the cell and is pinched off from the cell membrane. Dynamin 2 is thought to play a key role in altering the cell membrane to form these vesicles.

Dynamin 2 is also involved in the cell's structural framework (cytoskeleton). The protein interacts with multiple parts of the cytoskeleton, including tube-like structures called microtubules and proteins called actin, which organize into filaments to provide structure. These parts of the cytoskeleton are involved in movement of molecules within the cells, cell shape, cell mobility, and attachment of cells to one another.

Health Conditions Related to Genetic Changes

centronuclear myopathy

At least 24 mutations in the *DNM2* gene have been found to cause centronuclear myopathy, a condition that is characterized by muscle weakness (myopathy) in the skeletal muscles, which are the muscles used for movement. Most of these mutations change single DNA building blocks (nucleotides) in regions of the gene known as exon 8, exon 11, and exon 16. These mutations lead to a change in the structure of dynamin 2. *DNM2* gene mutations that cause centronuclear myopathy are described as "gain-of-function" because they appear to enhance the activity of dynamin 2, affecting endocytosis and leading to disorganization of structures similar to microtubules, called transverse tubules (T tubules), which are found within the membrane of muscle fibers. The T tubules are necessary for normal muscle tensing (contractions) and relaxation. As a result of the *DNM2* gene mutations, the structure of muscle cells becomes abnormal and they cannot contract and relax normally, leading to the muscle weakness that is characteristic of centronuclear myopathy.

Charcot-Marie-Tooth disease

Researchers have identified a few *DNM2* gene mutations that cause a form of Charcot-Marie-Tooth disease known as dominant intermediate B. Charcot-Marie-Tooth disease is a group of progressive disorders that affect the peripheral nerves,

which connect the brain and spinal cord to muscles and to sensory cells that detect sensations such as touch, pain, heat, and sound. Damage to the peripheral nerves can result in loss of sensation and wasting (atrophy) of muscles in the feet, legs, and hands.

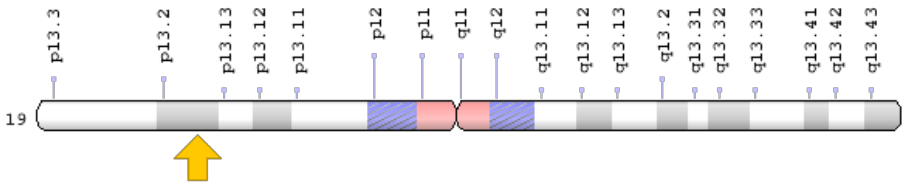
In addition, at least three *DNM2* gene mutations have been identified in individuals with another form of Charcot-Marie-Tooth disease called type 2. These mutations change or delete a single amino acid in dynamin 2.

DNM2 gene mutations that cause Charcot-Marie-Tooth disease are described as "loss-of-function" because they impair the activity of the dynamin 2 protein. These mutations may disrupt endocytosis, interfere with the arrangement of microtubules in the cytoskeleton, and disturb cellular organization. Researchers suggest that the mutations may also cause dysfunction of the Schwann cells that surround nerves. Schwann cells form myelin sheaths, which are the fatty coverings that insulate and protect certain nerve cells and promote the efficient transmission of nerve impulses. It is unclear how *DNM2* gene mutations cause the signs and symptoms of Charcot-Marie-Tooth disease.

Chromosomal Location

Cytogenetic Location: 19p13.2, which is the short (p) arm of chromosome 19 at position 13.2

Molecular Location: base pairs 10,718,053 to 10,831,910 on chromosome 19 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CMT2M
- CMTDI1
- CMTDIB
- DI-CMTB
- DYN2

- DYN2_HUMAN
- dynamin II
- DYNII

Additional Information & Resources

Educational Resources

- Annual Reviews Collection (2000): Dynamin and its Role in Membrane Fission
  https://www.ncbi.nlm.nih.gov/books/NBK2233/
- The Cell: A Molecular Approach (second edition, 2000): Endocytosis
  https://www.ncbi.nlm.nih.gov/books/NBK9831/

GeneReviews

- Charcot-Marie-Tooth Hereditary Neuropathy Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1358
- DNM2-Related Intermediate Charcot-Marie-Tooth Neuropathy
  https://www.ncbi.nlm.nih.gov/books/NBK45014

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28DNM2%5BTIAB%5D%29+OR+%28dynamin+2%5BTIAB%5D%29%29+OR+%28%28DYN2%5BTIAB%5D%29+OR+%28dynamin+II%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- DYNAMIN 2
  http://omim.org/entry/602378

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_DNM2.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=DNM2%5Bgene%5D
- HGNC Gene Family: Pleckstrin homology domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/682

- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=2974
- Inherited Peripheral Neuropathies Mutation Database
  http://www.molgen.ua.ac.be/CMTMutations/Mutations/Mutations.cfm?Context=38
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/1785
- UniProt
  http://www.uniprot.org/uniprot/P50570

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https://ghr.nlm.nih.gov/gene/DNM2

Reviewed: November 2015
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
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